UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/597,395	07/24/2006	Yulin Ren	27211/04220	1395

24024 7590 12/01/2010

CALFEE HALTER & GRISWOLD, LLP
800 SUPERIOR AVENUE
SUITE 1400
CLEVELAND, OH 44114

EXAMINER	
KRISHNAN, GANAPATHY	
ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
12/01/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ipdocket@calfee.com
dcunin@calfee.com

Office Action Summary	Application No.	Applicant(s)	
	10/597,395	REN ET AL.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,12-19 and 23-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,12-19 and 23-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 9/15/2010 has been received, entered and carefully considered. The following information has been made of record in the instant amendment:

1. Claims 9-11 and 20-22 have been canceled.

2. New Claims 30-31 have been added.

3. Claims 1, 5, 7-8, 13, 16, 18-19 have been amended.

4. Remarks drawn to rejections under 35 USC 103(a).

The following have been overcome:

5. In view of applicants arguments the rejection of Claims 1-8, 12-19 and 23-29 under 35 U.S.C. 103(a) as being unpatentable over Khanbabaee et al (Tetrahedron, 1997, 53(1), 10725-32) in view of Experimental Organic Reactions (1957, 18, pages 504-505, English Translation) has been withdrawn.

Khanbabaee et al have separated the alpha and beta isomers of the benzylated derivatives of PGG via chromatography and then converted them to the individual isomers of PGG. Experimental Organic Reactions teaches in general that racemic modifications can be separated by crystallization. The separation of benzylated derivatives by chromatography is not a suggestion that the non-benzylated derivatives can be separated by recrystallization of the anomers from a mixture.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-6. 8, 12-17, 19 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the step of filtering out any undissolved particles, originally recited as step (c). It is known in the art that undissolved particles can interfere and prevent crystallization of the desired product. Applicants have to insert the recitation "the step of filtering out any undissolved particles" in claims 1 and 13.

Claims 2-6, 12, 13-17, 19 and 23 which depend from a rejected base claim that is incomplete for omitting essential elements, such omission amounting to a gap between the elements are also rejected for the same reasons.

Claims 1-8, 12-19 and 23-31 are pending in the case.

The following new art rejection is made of record.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8, 12-19 and 23-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Farag et al (Bull. Pharm. Sci. Assiut University, 1998, 21(1), 1-6, newly cited) and Feldman et al (Phytochemistry, 1999, 51, 867-72, newly cited), in view of Pfeffer et al (US 4.107,425, newly cited), Experimental Organic Reactions (1957, 18, pages 504-505, English Translation, of record) and Ault (Techniques and Experiments for Organic Chemistry, 1987, pages 44-46, of record and pages 120-21, newly cited).

Farag et al teach the extraction and separation of the alpha and beta anomers of pentagalloyl glucose (PGG) existing as a mixture in a methanol extract. From this extract the individual alpha and beta isomers have been separated via chromatography using 2:1 water and methanol as solvents (page 2, left col., see Extraction and Fractionation; Isolation and compounds 3 and 4 on the right column). The major component is water. This indicates that there is a difference in solubility of the alpha and beta anomers of PGG in water and this can be taken advantage of for separation of the two anomers from a solution containing a mixture of the two anomers in water.

Feldman et al teach that the individual alpha and beta anomers of PGG is separated and purified for binding studies for each anomer (page 869, Table 1).

Farag et al. and Feldman et al do not specifically teach the separation of the alpha and beta anomers of pentagalloylglucose (PGG) from a mixture of the alpha and beta anomers using either water (instant claim 1) or acetone (instant claim 13) via crystallization as instantly claimed. However, according to the teaching of Farag and Feldman, the separation of the alpha and beta anomers of PGG is not only known in the art, but also alpha and beta anomers are known to have different properties and activities.

Pfeffer et al. teaches that using crystallization for the separation of the beta anomer of tetra-O-benzyl-1-hexadecanoyl-D-glucose from a mixture comprising an 11:89 ratio of the alpha and beta anomers, via from absolute ethanol (col. 5, line 45 through col. 6, line 13) is known in the art. This is separation of a single anomer (the beta anomer) from a mixture comprising 50% or more of the beta isomer and less than 50% of the alpha isomer as in instant claim 13. The steps used by Pfeffer are the same as recited in steps (a)-(c) in claims 1 and 13 and steps (a)-(d) in claims 24 and 27. One of ordinary skill in the art would use these same steps for the separation of the individual anomers of PGG via crystallization.

According to Experimental Organic Reactions (English translation of section 3.2) resolution of racemic modification (separation of anomers/optical isomers) can occur via recrystallization. Examples wherein water/methanol or acetone is used to separate racemates are disclosed (Translation, page 1, second paragraph). This means that alpha and beta anomers of PGG can also be separated via crystallization from a mixture using water and acetone as solvents

based on the differences in solubility of the anomers as seen in the teaching of Farag et al and such separation via crystallization of closely related derivatives as taught by Pfeffer.

According to Ault (Techniques and Experiments for Organic Chemistry, 1987, pages 120-21) the separation of compounds is based on the ability of the solvent used to selectively dissolve a substance that is to be separated (page 120, last paragraph). Separation depends on the difference in solvent power towards the substances (page 121, first two lines below Table). This indicates that the difference is solubility of substances in a solvent can be used for separating a mixture via crystallization also. In the instant case such a difference is seen in the teaching of Farag et al for the alpha and beta anomers of PGG. Based on the teaching of Farag, Pffeffer and Ault a reasonable expectation of success is seen for separating the alpha and beta anomer of PGG using water and acetone as solvents.

At pages 44-46 Ault teaches that in the process of crystallization of a solid from a solvent, the compound is dissolved in the solvent and the resulting solution is filtered to remove undissolved material (page 46, Fig. 8.1; steps recited in claims 30-31). This is a step that is used in all crystallizations wherein undissolved material is present. Hence, one of ordinary skill in the art would use this step in the instant process if undissolved material is present. One of ordinary skill in the art knows well that such undissolved material if not removed before the cooling step could prevent the desired compound from crystallizing out of solution. Ault also teaches that after the compound is added to the solvent it should be warmed up if necessary to dissolve it completely in the solvent (page 46, last paragraph). This is same as the steps recited in instant claims 5-6, 8, 16-17 and 19. Therefore, based on the teaching of the prior art above the

separation of the alpha and beta isomers of PGG using the solvents as instantly claimed is predictable and one of ordinary skill in the art would use recrystallization to separate the isomers.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to separate the alpha and beta anomers of penta-O-galloyl-D-glucose from a mixture of the alpha and beta anomers via the method as instantly claimed since analogous separations of the alpha and beta anomers of glucose derivative structurally similar to pentagalloyl glucose via crystallization using water/methanol or acetone as solvents have been disclosed in the prior art. Therefore the prior art shows that it is possible to separate the alpha and beta anomers of the pentagalloyl derivative of glucose.

One of ordinary skill in the art would be motivated to use the method as instantly claimed since separation of anomers via crystallization is a well known technique and as disclosed in the art readily available solvents like water and acetone have been successfully used for such separations. One of ordinary skill in the art would expect the separation of the alpha and beta galloyl derivatives of glucose to also take place with a reasonable expectation of success based on the disclosure of the prior art.

MPEP 2141 states, "The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in KSR noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Court quoting In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006), stated that "[R]ejections on obviousness cannot be sustained by mere conclusatory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.'" KSR, 550 U.S. at ,82 USPQ2d at 1396.

Exemplary rationales that may support a conclusion of obviousness include: (A) Combining prior art elements according to known methods to yield predictable results; (B) Simple substitution of one known element for another to obtain predictable results; (C) Use of known technique to improve similar devices (methods, or products) in the same way; (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results; (E) " Obvious to try " choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success; (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art; (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention."

Rationales (A), (C) and (E) are applicable in this case. The prior art teaches the use of water and acetone for separating components from a mixture via crystallization using these two solvents, which are also used in the instant method. In the instant case separation of the alpha and beta anomers by choosing a known method (crystallization) and choosing a solvent for crystallization from a finite number of choices disclosed in the prior art with a reasonable expectation of success, according to KSR renders the instant claims obvious. Also the teaching of Farag shows that difference in solubility between two substances (alpha and beta anomers of PGG in the instant case) can also be used to separate them from a mixture via crystallization since difference in solubility is a property known in the art for separating individual components from a mixture via crystallization.

"Aventis Pharma Deutschland v. Lupin Ltd., 499 F.3d 1293 (Fed. Cir. 2007). A chemical compound would have been obvious over a mixture containing that compound as well as other compounds where it was known or the skilled artisan had reason to believe that some desirable property of the mixture was derived in whole or in part from the claimed compound, and separating the claimed compound from the mixture was routine in the art."

In the instant case separating the alpha and beta isomers of PGG is known in the art as explained above.

It is well within the skill level of the artisan to prepare a single crystal of the respective anomers via the same crystallization technique and using the same solvents from samples that are greater than 95% pure since PGG is known in the art to have beneficial effects (as disclosed in the Background section in the Specification) and one of ordinary skill in the art would use the known separation technique disclosed in the art to separate the isomers in order to look at the activity of the individual isomers. It is also well within the skill level of the artisan to adjust the ratio of the solvent to the product to be crystallized, the duration of cooling to obtain crystals, the type of filter paper to be used for separating the crystals, etc. in order to recover the maximum amount of the pure anomer from the crystallizing solution.

Conclusion

Claims 1-8, 12-19 and 23-31 are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ganapathy Krishnan/
Examiner, Art Unit 1623

/Shaojia Anna Jiang/

Supervisory Patent Examiner, Art Unit 1623